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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/605,577 06/28/00 WANG

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EXAMINER

SEHARASEYON, J

ART UNIT

PAPER NUMBER

1647

DATE MAILED:

3
10/26/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/605,577

Applicant(s)

WANG ET AL.

Examiner

Jegatheesan Seharaseyon

Art Unit

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- 1) ☒ Responsive to communication(s) filed on 26 September 2000.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some * c) ☐ None of the CERTIFIED copies of the priority documents have been:
1. ☐ received.
2. ☐ received in Application No. (Series Code / Serial Number) _____.
3. ☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2.
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

DETAILED ACTION

1. Claims 1-10 are pending and under consideration by the examiner.

Specification

2. The diagrams have been approved by the draftsman.

Claim Rejections - 35 USC § 112 first paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3a. Claims 1-7 are rejected because the specification, while being enabling for a stable pharmaceutical composition comprising human interleukin-2 or a variant (N88R), does not reasonably provide enablement for a composition comprising other IL-2 variants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-7 recite a composition comprising an "IL-2 variant". There is no guidance provided in the specification as to how one of ordinary skill in the art would generate a composition comprising an IL-2 variant, other than the one exemplified in the specification. The specification is non-enabling for any other IL-2 variants other than N88R. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is

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not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Given the breadth of claims 1-7 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use an IL-2 variant as claimed.

Claim Rejections - 35 USC § 112 second paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

PM 10/23/09 Claims 1, 4-7, 8, and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4a. Claim 1 is rejected as vague and indefinite for reciting the term "variant", because

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the term "variant" is not defined in the specification. Therefore the metes and bounds of this claim are unclear. This is because a variant may encompass a single amino acid change or several amino acid changes and it is unclear what "variants" are encompassed in this claim.

4b. Claims 4-6 are rejected as vague and indefinite for reciting the term "including" , because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

4c. Claim 7 is rejected as vague and indefinite for reciting the term "mutein", because the specification does not clearly define the term "mutein". The muteins described could be deletion, substitution, addition of a single amino acid or more than one amino acid.

4d. Claims 8 and 10 are rejected as vague and indefinite for reciting the term "N88R" because the full meaning of an acronym should be spelled out at its first use in any claim.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5a. Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over

Hora et al. (U.S. Patent No. 5,078,997), in view of Lee (U.S. Patent No. 5,656,730).

Hora et al. teaches the stabilization of IL-2 with sugars, amino acids, vitamins, fatty acids, polymers or low molecular weight acids (page 6, lines 11-60). Hora et al. also teaches the reconstitution of the lyophilized protein in water (page 8, lines 30-34). In addition, the reference teaches of a stable pharmaceutical composition maintained at a pH between 5 and 8.5 (page 5, lines 31-34). Hora et al. does not expressly disclose the use of histidine and/or glycine to stabilize the pharmaceutical compositions.

Lee discloses the use of sucrose, histidine and/or glycine combinations to stabilize a monomeric protein composition (page 6, lines 35-44). Therefore, it would have been obvious to one having ordinary skill in the art at the time the instant invention was made to modify the composition disclosed in Hora et al. with the addition of sucrose, histidine and/or glycine as disclosed in Lee. Since, Lee teaches that the addition of sucrose, histidine, and glycine stabilize monomeric proteins (page 6, lines 35-44). In claims 7 and 8 it is expected that the mutein of IL-2 would be stabilized similar to wild type IL-2.

5b. Claims 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hora et al. (U.S. Patent No. 5,078,997), in view of Nayar (U.S. Patent No. 5,874,408). The disclosure of Hora et al. has been set forth above in paragraph 5a. However, Hora et al. does not expressly disclose the use of histidine and glycine to stabilize the pharmaceutical compositions. Furthermore, it also does not teach use of NaCl in the composition.

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Nayar discloses the use of sucrose, histidine, glycine and NaCl combinations to stabilize plasma protein compositions (page3, lines 20-30). Therefore, it would have been obvious to one of ordinary skill in the art at the time, the instant invention was made to modify the composition disclosed in Hora et al. by adding the additional elements disclosed in Nayar, because the reference teaches that the addition of sucrose, histidine, glycine and NaCl stabilize plasma proteins. In claim 10, the expectation is that the reconstituted composition of mutein will be similar to that of wild type IL-2.

Conclusion

6. No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 703-305-1112. The examiner can normally be reached on M-F: 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-0294 for regular communications and 703-308-4227 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

JS
October 23, 2000

Prema Mertz
PREMA MERTZ
PRIMARY EXAMINER